POC INR Device Evaluation

Virginia POC Network
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Brad S. Karon, MD, PhD
Associate Professor of Laboratory Medicine and Pathology
Mayo Clinic
Rochester, MN
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Learning objectives

• Define the issues to consider when choosing point of care INR devices

• List the advantages and disadvantages to measuring INR at the point of care

• Describe differences in accuracy between common point of care INR systems
Outline

• Why monitor warfarin therapy
• Pros and cons of point of care INR
• Choosing POC INR devices
• Conclusions
A question for you...
Why monitor warfarin

• Warfarin mechanism of action
Why monitor warfarin

- Major indications for warfarin therapy
- Primary & secondary prevention of venous thromboembolism
- Prevention of systemic embolism in patients with prosthetic heart valves or atrial fibrillation
Why monitor warfarin

• Narrow therapeutic window
• Variability in patient response
  Genetics
  Co-morbidities
• Drug and diet interactions
• Variability in laboratory testing methods
• Time delay (~1 day) between dosing and ability to measure response
Why monitor warfarin

• Target INR 2.0 – 3.0
  INR 4.5: 2-3 fold increase in risk of bleeding
  INR 5.5: 5 fold increase
  INR >6.0: 8-10 fold increase
Why monitor warfarin
Optimal Anticoagulation
for Mechanical Heart Valves

Event Rate (per 100 patient years)

PT-INR

Thromboembolism
Observed

Hemorrhage
Observed

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Why monitor warfarin

Variability in patient response

- Drugs, dietary supplements or herbal medicines
  - Changes in absorption or clearance of warfarin
  - Changes in synthesis or clearance of vitamin K dependent factors
  - Interference with other pathways of hemostasis (e.g., platelet function)
Why monitor warfarin
Variability in patient response

- Diet and dietary supplements
  Higher content of vitamin K

- Disease
  Hepatic dysfunction
    Impaired synthesis of coagulation factors
  Hypermetabolic states (e.g., fever)
    Increased catabolism of factors
Why monitor warfarin
Variability in patient response

• Artifact of testing variability

Thromboplastins vary in responsiveness to coagulation factor deficiency
Different instrument reagent combinations can give different results
Protime (PT) values differ markedly between instrument/platform combinations
Standardization to the INR, but it’s not perfect
  \[ \text{INR} = \left( \frac{\text{PT (patient)}}{\text{PT (geomean)}} \right)^{\text{ISI}} \]
Thromboplastins with different ISI values tend to differ more in INR values
Why monitor warfarin

- Ortho RecombiPlasTin (ISI 1.05) at 0 h
- Dade Thromboplastin C-Plus (ISI 1.85) at 0 h
- Dade Innovin (ISI 0.85) at 0 h

Why monitor warfarin
Reasons for INR inaccuracy

• Based on ISI values derived from patients on stable anticoagulation
  Results less reliable early in therapy

• Instrument/reagent combinations

• Incorrect ISI

• Preanalytical variables
Why monitor warfarin

- Goal is to prevent venous thromboembolism while minimizing the risk of hemorrhage
  - Setting the right target range
  - Getting to the right target quickly
  - Staying in the therapeutic range as much as possible
Why monitor warfarin

- Times of increased risk with sub- or supra-therapeutic levels
  
  Initiation of therapy
  Changes in medications and/or diet
  Illness, hospitalization
  Change of testing laboratory
  Transitions of care
    - Hospital discharge
    - Provider change
Why monitor warfarin

• Success and safety of therapy contingent upon
  Patient knowledge & compliance
    Education opportunities during therapy/measurement
  Provider knowledge, experience & diligence
    Need to follow up after INR result for treatment recommendation?

Systems of care delivery
How good is system at ensuring INR measurement at correct time/intervals, recommendations for treatment reach patient, patient understands recommendations
A question for you...
Pros and Cons

• When might POC INR program add value?

When POC INR is reasonably accurate compared to local INR reference method

When system for warfarin monitoring is improved in POC compared to non-POC environments

Real time education
Real time warfarin dosage adjustment
Better patient compliance monitoring
Better patient outcome
Pros and Cons

• **Pros**
  - Rapid turnaround time—allows real-time education and dose adjustment
  - Easy to use
  - Some waived
  - Accessible
  - No venipuncture

• **Cons**
  - Comparability to laboratory methods
  - Outliers/fliers
  - Cost
  - Oversight issues
  - Interferences (LMWH)
  - Response during initiation/termination of therapy

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Pros and Cons

• Major studies comparing home INR monitoring with lab monitoring

• Heneghan et al., Lancet 2006;367:404-11

Systematic review of 14 randomized trials of self-monitoring vs. routine care for INR adjustment

Self monitoring and adjustment reduced risk of thromboembolism and all-cause mortality but did not significantly reduce risk of major hemorrhage
Pros and Cons

• Major studies comparing home INR monitoring with lab monitoring

• THINRS randomized study of 2922 VA patients (N Engl J Med 2010;363:1608-20)

  Randomized patients to weekly home testing vs. monthly high quality clinic testing

  No advantage of home testing in terms of rates of thromboembolism, slightly more bleeding in POC group

  Patients preferred home testing

  Not a comparison of home INR vs. routine care
Choosing POC INR devices

- Technical performance
  - Equivalency to your laboratory method – bias
  - Reproducibility with intended sample type
    - Intra & inter device
  - Cutoff for requiring confirmatory lab result
  - Performance at key decision point(s)

- Health care setting
  - Number and commitment of users
  - Patient populations (hospice, nursing home, oncology clinic, pediatric clinic, etc)
    - Stably anticoagulated? Able to understand instructions?
    - Reasons for anticoagulation?
  - Frequency of concurrent heparin use
  - System for management dependent upon POC application
Choosing POC INR Monitors

• Varying thromboplastins (ISI) and endpoint detection methods
• Designed to use capillary whole blood
• Designed primarily for patient use
• Data management capabilities to enhance professional use just starting to be available
Choosing POC INR Monitors

• Data on accuracy/precision of POC INR devices
• Many studies published
• Focus on those comparing capillary whole blood (POC) to plasma INR (lab) if that is intended use
• Note lab reference method used
• Look at decision thresholds and concordance in similar decision range
Choosing POC INR Monitors

• Mayo Study of 3 devices

• Study period one:
  50 patients had both Method A and Method B
  POC INR by capillary fingerstick (separate
  fingersticks), and lab analysis by venipuncture
  for plasma INR on MDA 180 using Innovin
  thromboplastin

• Study period two:
  50 patients had both Method A and Method C
  POC INR by capillary fingerstick (separate
  fingersticks) and lab analysis of plasma INR
Results: Study period one
Method A vs. lab plasma

Median bias = 0.0 INR units

5 of 50 exceeded 0.5 INR units of reference method
Results: Study period one
Method B vs. lab plasma

Median bias = -0.1 INR units
1 of 50 exceeded 0.5 INR units of reference method
Results: Study period two
Method A vs. lab plasma

Median bias = -0.2 INR units (statistically sig difference from Method A performance during Period 1)
3 of 48 exceeded 0.5 INR units of reference method
Results: Study period two
Method C vs. lab plasma

Median bias = 0.0 INR units
1 of 48 exceeded 0.5 INR units of reference method
Overall distribution of results vs. reference plasma method

> 90% of POC results within 0.4 INR units of reference for Methods B and C
Study Conclusions

• Both Methods B and C capillary whole blood INR are closely correlated with plasma INR using Innovin

• Performance of capillary whole blood INR devices changes over time (relative to lab plasma), indicating a need for ongoing quality control/proficiency testing of these devices

• Lessons learned: Choose method with little systematic bias vs. lab reference, but don’t assume continued accuracy/bias over time
Older Mayo method comparison

- Don’t assume that every method will match your lab
Precision assessment for POC INR

• Data from stabilized QC material overestimates precision

• If possible look at intra and inter-device precision using duplicate measurements from capillary fingersticks
Precision assessment for POC INR

> 90% repeat fingerstick INR measurements within 0.4 INR unit whether done with same or different device
Choosing POC INR Monitors

• Look for minimal (≤ 0.2 INR unit) systematic bias between POC capillary and lab plasma INR

• Look for maximum clinical concordance, generally measured as % values within 0.4-0.5 INR units

• Look for minimal outliers (≥ 1.0 INR unit), though outliers may be due to user or instrument errors

• Interference by heparin and LMWH, product labeling and data

• Range of hematocrits, labeling and data

• Data management

• Meaningful precision data difficult to gather
A question for you...
QUESTIONS and COMMENTS?